

NSABP B-43: A Phase III Clinical Trial Comparing Trastuzumab Given Concurrently with Radiation Therapy and Radiation Therapy Alone for Women with HER2-Positive Ductal Carcinoma In Situ Resected by Lumpectomy

Fast Facts

Patient selection guidelines

Although the guidelines in Section 4.1 are not inclusion/exclusion criteria, investigators should consider each of these factors when selecting patients for B-43. Investigators should also consider all other relevant factors (medical and non-medical), as well as the risks and benefits of the study therapy when deciding whether a patient is appropriate for B-43. These considerations should be weighed carefully, as they may make a patient an unsuitable candidate for B-43 and may increase risk to the patient.

- Pre-entry central HER2 testing (see Sections 6.1 and 6.2 and Appendix C) is required for all patients. The correlative studies are required for all patients enrolled in B-43 (see Appendix D). Therefore, **submission of a representative tumor block for the B-43 trial is required. Submission of alternative tissue samples is NOT permitted.** The local pathology department policy regarding release of blocks must be considered when screening patients.
- Patients with a life expectancy of less than 10 years, excluding the diagnosis of ductal carcinoma in situ of the breast. (Comorbid conditions should be taken into consideration, but not the DCIS diagnosis.)
- Women of reproductive potential must agree to use an effective non-hormonal method of contraception during therapy **and for at least 6 months after completion of trastuzumab.**
- Psychiatric or addictive disorders or other conditions that, in the opinion of the investigator, would preclude the patient from meeting the study requirements.

Eligibility Criteria

1. The patient must have consented to participate and must have signed and dated an appropriate IRB-approved consent form that conforms to federal and institutional guidelines *for the study treatment and for the pre-entry tumor block submission* for HER2 testing and B-43 correlative studies (see Section 6.1).
2. Patients must be female.
3. Patients must be 18 years of age or older.
4. Patients must have an ECOG performance status of 0 or 1
5. On histologic examination, the tumor must be ductal carcinoma in situ (DCIS). (Patients with mixed DCIS and lobular carcinoma in situ [LCIS] are eligible.)
6. The DCIS must be HER2-positive as **determined by central testing** (see Sections 6.1 and 6.2 for details).
7. Estrogen and/or progesterone receptor status must be determined prior to randomization. (Patients with DCIS that is hormone receptor positive or negative are eligible.)
8. All DCIS must have been resected by lumpectomy.
9. The margins of the resected specimen must be histologically free of DCIS. For patients in whom pathologic examination demonstrates DCIS present at the line of resection, re-excision(s) may be performed to obtain clear margins. (Patients who require mastectomy are not eligible.)
10. If axillary staging is performed, nodal staging must be pN0, pN0(i-), pN0(i+) which is defined as isolated tumor cells ≤ 0.2 mm, regardless of the method of detection, i.e., IHC or H&E, pN0(mol-), or pN0(mol+). **Note: Axillary staging is not required.**
11. The interval between the last surgery for excision of DCIS (lumpectomy or re-excision of lumpectomy margins) and randomization must be no more than 120 days.

Ineligibility Criteria

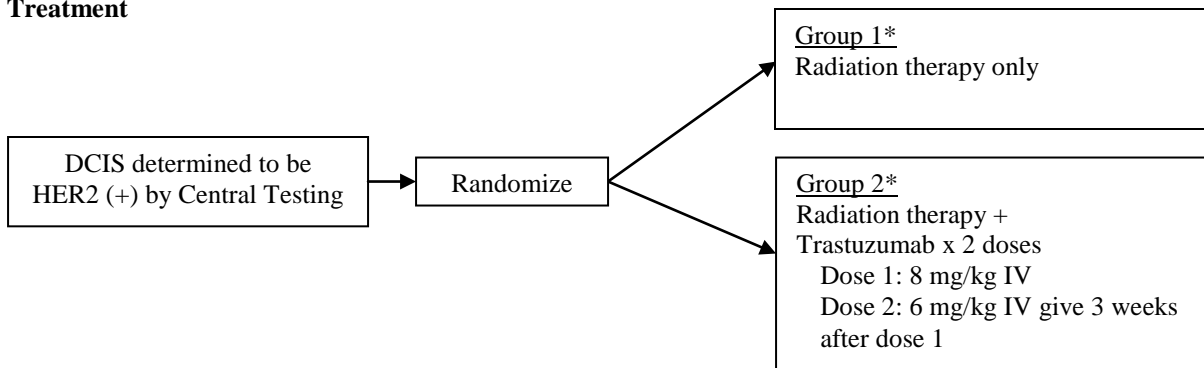
1. Invasive (including microinvasion staged as T1mic) breast cancer. (Patients with DCIS "suspicious" for microinvasion, but not confirmed, are eligible.)
2. Nodal staging of pN1 (including pN1mi). (Note: Axillary staging is not required.)
3. DCIS present in more than one quadrant (multicentric).

4. Masses or clusters of calcification that are clinically or mammographically suspicious unless biopsied and proven to be benign. (If DCIS is found, the patient is eligible if the DCIS was in the same quadrant of the ipsilateral breast and was resected with clear margins.)
5. Contralateral breast cancer (including DCIS).
6. Whole breast irradiation administered before randomization. (Partial breast irradiation is prohibited.)
7. Prior history of breast cancer, including DCIS. (Patients with a history of LCIS are eligible.)
8. Prior anthracycline chemotherapy for any malignancy.
9. Cardiac disease that would preclude the use of the drugs included in the B-43 treatment regimens. This includes but is not confined to:
Active cardiac disease:
 - angina pectoris that requires the use of anti-anginal medication;
 - ventricular arrhythmias except for benign premature ventricular contractions (PVCs) controlled by medication;
 - conduction abnormality requiring a pacemaker;
 - supraventricular and nodal arrhythmias requiring a pacemaker or not controlled with medication; and
 - clinically significant valvular disease.*History of cardiac disease:*
 - myocardial infarction documented by elevated cardiac enzymes or persistent regional wall abnormalities on assessment of LV function;
 - documented congestive heart failure; or
 - documented cardiomyopathy.
10. Uncontrolled hypertension, i.e., systolic BP greater than 180 mm/Hg and/or diastolic BP greater than 100 mm/Hg. (Patients with hypertension that is well controlled on medication are eligible.)
11. Other nonmalignant systemic disease that would preclude a patient from receiving trastuzumab or radiation therapy or would prevent prolonged follow-up.
12. Other malignancies unless the patient is considered to be disease-free for 5 or more years prior to randomization and is deemed by her physician to be at low risk for recurrence. Patients with the following cancers are eligible if diagnosed and treated within the past 5 years: carcinoma in situ of the cervix, carcinoma in situ of the colon, melanoma in situ, and basal cell and squamous cell carcinoma of the skin.
13. Pregnancy or lactation at the time of study entry. (*Note: Pregnancy testing according to institutional standards should be performed for women of childbearing potential.*)
14. Administration of any investigational agent within 30 days before study entry.

Pre-Study Parameters

1. History and physical exam including height and weight, menopausal status, menopausal history
2. Radiation oncology evaluation (post-operative)
3. Pregnancy test for women of child bearing potential
4. Bilateral mammogram within 6 months
5. Central HER2 testing of tumor block

Treatment



*Hormone receptor positive patients should receive minimum of 5 year hormonal therapy. Trastuzumab provided.